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I. General Information

CAS Number: 94-60-0*
Name: 1,4-Cyclohexanedicarboxylic acid, dimethyl ester
Dimethyl cyclohexane-1,4-dicarboxylate
Dimethyl-1,4-cyclohexanedicarboxylate
Dimethyl hexahydroterephthalate
DMCD (mixed isomers)

* This CAS No. is a mixture of both *cis*- and *trans*- isomers. The chemical CAS number used for some tests was 3399-22-2, which corresponds to a pure *trans*- isomer of DMCD.

II. Physical-Chemical Data

A. Melting Point

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	
Method	
Method:	Estimation
Remarks:	
Results	
Melting point value:	-46.41 °C
Remarks:	Data is a mean of both estimation methods
References	MPBPWIN v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

B. Boiling Point

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	Purity unknown
Method	
Method:	Not Specified
GLP:	Unknown
Year:	Unknown
Results	
Boiling point value:	265 °C (mixed isomer)
Pressure:	Not stated
Remarks:	Primary reference was not obtained.
References	Lewis, R.J., Sr (Ed.). Hawley's Condensed Chemical Dictionary. 12th ed. New York, NY: Van Nostrand Rheinhold Co., 1993, 415.
Other	Data obtained from Hazardous Substances Data Bank Number: 5284. Last revision date: 20010809.

C. Vapor Pressure

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	
Method	
Method:	Estimation
Remarks:	Modified Grain method and Antoine method. Results are a mean of both methods.
Results	
Vapor pressure value:	0.0822 mmHg
Temperature:	25 ^{o}C
Remarks:	
References	MPBPWIN v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

D. Partition Coefficient

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	
Method	
Method:	Estimation
Remarks:	
Results	
Log K_{OW}:	2.11
Remarks:	
References	KOWIN v1.66; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

E. Water Solubility

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	
Method	
Method:	Estimation
Remarks:	
Results	
Value:	688.7 mg/L
Temperature:	25 ^{o}C
Description:	Slight
Remarks:	A K_{ow} of 2.11 was used in the estimation
References	WSKOW v1.40; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	
Method	
Method:	Estimation
Test type:	Atmospheric oxidation
Remarks:	
Results	
Temperature:	25 ^{o}C
Hydroxyl radicals reaction	
OH Rate constant:	7.9071 x 10^{-12} cm^3/molecule-sec
Half-life	1.35 Days (12-hr day; 1.5x10^6 OH/cm^3)
Ozone reaction:	No ozone reaction estimation
Remarks:	
Conclusions	Material is oxidized at a moderate rate by hydroxyl radicals in the atmosphere.
Data Quality	
Remarks:	
References	AopWin v1.90; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

B. Stability in Water

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	Test material is an ester compound
Method	
Method:	Estimation
Test type:	Aqueous base/acid-catalyzed hydrolysis
Temperature:	25 ^{o}C
Remarks:	
Results	
Total K_b for pH >8:	2.423 x 10^{-2} L/mol-sec
Half-life (pH 8):	331.018 days
Half-life (pH 7):	9.063 years
Remarks:	Material is not likely to be hydrolyzed by surface water.
References	HYDROWIN v1.67; Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210.
Other	

C. Biodegradation

Test Substance	
Test substance:	DMCD (*trans* isomer); CAS No.: 3399-22-2
Remarks:	Purity was 99.9%
Method	
Method:	OECD:TG-301B and Annex V C.5
Test type:	Ready biodegradation using the CO_2 evolution test (Modified Sturm)
GLP:	Yes
Year:	1991
Contact time:	35-days
Inoculum:	Activated sludge microorganisms (unacclimated)
Remarks:	Activated sludge was obtained from Van Lare Treatment plant in Rochester NY. Four inoculated carboys were used: one for the inoculum blank, one for a positive control (sodium benzoate), and two containing test article (tested at 10 and 20 mg/L). Microbe count of supernatant was 10^7 organisms/ml.
Results	
Total degradation at test end (Day 35):	81% (10 mg/L) and 79% (20 mg/L)
Time for 10% degrad.:	11 days
Does study meet 10-day window criteria:	No
Classification:	Results indicate material was not readily degraded (>60%) within the 10-day time frame
Breakdown products:	Not determined
Remarks:	No significant amount of CO_2 was evolved from inoculum blank. The positive control reached 60% degradation by Day 8 and 79% by test end (DOC loss was therefore 98%). DMCD was not readily biodegradable according to the definitions of this test which requires >60% degradation within the time window of 10 days, counting from the day that the observed level of biodegradation first exceeds 10%. Instead, DMCD was only degraded 54% (10 mg/L) and 48% (20 mg/L) in this time frame but considerable biodegradation did occur, however, based on 60% degradation within a 12-day time window. The end of the test on Day 35 observed 81% biodegradation of DMCD at 10 mg/L and 79% at 20 mg/L.
Conclusions	These data indicate DMCD is unlikely to persist in the environment but it may not be fully removed during wastewater treatment.
Data Quality	
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Ready Biodegradability (Modified Sturm); Environmental Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-105-043461-1, November 14, 1991.
Other	An activated sludge respiration inhibition test was conducted on *trans*-DMCD following OECD guidelines 209/1988 Annex V supplement and GLP assurances. Results determined the NOEC to be 1000 mg/L (highest dose tested). [Environmental Sciences Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-620-043461-1, August 1991.

D. Transport between Environmental Compartments (Fugacity)

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	
Method	
Test type:	Estimation
Model used:	Level III Fugacity Model; EPIWIN:EQC from Syracuse Research Corporation
Remarks:	
Results	
Model data and results:	Distribution (%)
Estimated distribution and media concentration (levels II/III):	Air 1.32 Water 35.6 Soil 63.0 Sediment 0.119
Remarks:	Physical chemical values utilized in this model were default values obtained from the EPIWIN program.
Conclusions	
Data Quality	
Remarks:	
References	Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15(9)**, 1618-1626 and 1627-1637.
Other	

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance	
Test substance:	DMCD (*trans* isomer); CAS No.: 3399-22-2
Remarks:	Purity was 99.9%
Method	
Method:	EPA 600/3-75-009 and 600/4-85/013, 3rd Ed.
Test type:	Acute: Static w/ renewal at 48 hours
GLP:	No
Year:	1991
Species/strain:	Fathead minnow (*Pimephales promelas*)
Analytical monitoring:	Yes; temperature, pH, dissolved oxygen, alkalinity, hardness, conductivity
Exposure period:	96-Hours
Remarks:	Moderately hard reconstituted water used as control and dilution water. Two replicates of 500 mL solution in 1000 mL glass beakers containing 10, 48-day old fish used per treatment level. Test conducted at 24 ± 1 ^{o}C.
Results	
Nominal concentration:	10, 18, 32, 56, 100 mg/L
Measured concentration:	Not measured
Endpoint value:	96-hour LC_{50} = 23 mg/L
Biological observations:	No mortality was observed throughout the 96-hour exposure in the control. Several fish at the 18 & 32 mg/L treatment level exhibited loss of equilibrium
Statistical methods:	Trimmed Spearman-Karber Method
Remark:	Although concentrations were not measured, data from the algae study suggest the material remains in the test solution and does not volatilize or degrade.
Conclusions	The 96-hour LC_{50} value indicates that the test substance would be classified as "harmful to aquatic organisms" according to the European Union's labeling directive and would correspond to a "moderate concern level" according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	This was a well-documented study conducted using USEPA methodology but without concentration verification of test material.
References	Aquatic Toxicity of Trans-DMCD to *Pimephales promelas, Daphnia magna*, and *Ceriodaphnia dubia*; Young-Morgan & Associates, Franklin, Tennessee; August 1991.
Other	

B. Acute Toxicity to Aquatic Invertebrates

Test Substance	
Test substance:	DMCD (*trans* isomer); CAS No.: 3399-22-2
Remarks:	Purity was 99.9%
Method	
Method:	EPA 600/3-75-009 and 600/4-85/013, 3rd Ed.
Test type:	Acute
GLP:	No
Year:	1991
Species/strain:	Daphnia magna
Analytical monitoring:	Yes; temperature, pH, dissolved oxygen, alkalinity, hardness, conductivity
Exposure period:	48-Hours
Test details:	Moderately hard reconstituted water used as control and dilution water. Two replicates of 50 mL solution in 100 mL glass beakers containing 10 neonates were used per treatment level. Test was conducted at 24 ± 1 ^{o}C.
Remarks:	
Results	
Nominal concentration:	10, 18, 32, 56, & 100 mg/L
Measured concentration:	Not measured
Endpoint value:	48-hour LC_{50} > 100 mg/L
Biological observations:	Only one mortality in the 100 mg/L treatment was observed in the test. No mortality was observed in the control or other treatment levels
Statistical methods:	NA
Remarks:	Although concentrations were not measured, data from the algae study suggest the material remains in the test solution and does not volatilize or degrade.
Conclusions	The 48-hour LC_{50} value indicates that the test substance would not be classified according to the European Union's labeling directive and would correspond to a "low concern level" according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	This was a well-documented study conducted using USEPA methodology but without concentration verification of test material.
References	Aquatic Toxicity of Trans-DMCD to *Pimephales promelas, Daphnia magna*, and *Ceriodaphnia dubia*; Young-Morgan & Associates, Franklin, Tennessee; August 1991.
Other	

C. Toxicity to Aquatic Plants

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	Purity was 92.9% by weight determined by GC/FID. Structure confirmed by mass spectrometric detection
Method	
Method:	OECD: TG-201
Test type:	Growth inhibition of algae
GLP:	Yes
Year:	2003
Species/strain:	*Selenastrum capricornutum*
Endpoint basis:	Cell concentrations (biomass) and growth rate
Exposure period:	72-hours
Analytical procedures:	Temperature, light intensity, rpm, and test substance concentration were assessed at the 0, 24, 48, and 72 hours. The pH was assessed at time 0 and after 72 hours.
Remarks:	The concentration of algae at Day 0 was 10^4 cells/ml.
Results	
Nominal concentration:	125 mg/L
Measured concentration:	124.6 mg/L (geometric mean)
Endpoint value:	E_bC_{50} and E_rC_{50} (0-72 hr) > 124.6 mg/L
NOEC or LOEC:	72-hour NOEC = 124.6 mg/L
Was control response satisfactory:	Yes (a 129.9 fold increase in cell number was observed within 3 days)
Statistical Methods:	NA, The statistical analysis of the data was not necessary as inhibition in biomass or growth rate was not observed.
Remarks:	A mean illumination of 741 foot-candles was maintained. The mean temperature was 24°C and pH ranged from 7.56 to 7.88. Cultures were oscillated at 100 rpm. Test substance and cell concentrations were determined at test initiation and at 24-hour intervals during the test. The exposure concentration was calculated as the geometric mean of the test substance solutions analyzed at test start and at 24-hour intervals. The test substance was stable under the conditions of the test as 2.98% loss was observed over 72 hours. No protocol deviations were noted.
Conclusions	The 72-hour E_bC_{50} and NOEC values indicate that, based on this study, the test substance would not be classified according to the European Union's labeling directive and would be classified as a "low concern level" according to the U.S. EPA's assessment criteria.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was a well-documented OECD-study conducted under GLP assurances
References	A Growth Inhibition Test with the Alga, *Selenastrum capricornutum*; Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; Study No. EN-512-907570-A; February 26, 2003.
Other	

V. Toxicological Data

A. Acute Toxicity

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	Purity was not noted in report
Method	
Method:	OECD TG-401 (Annex V, test B.1)
Test type:	Acute lethality; LD_{50} estimate
GLP:	Yes
Year:	1996
Species/strain:	Rat/CD(SD)BR VAF/Plus
Route of exposure:	Oral gavage
Dose levels:	2,500, 4,000, and 5,000 mg/kg
Remarks:	There were five/sex at 5,000 mg/kg and 5 females for 2,500, 4,000 mg/kg. Animals were 7-8 weeks in age and weighed between 200-214 (males) and 155-184 (females) grams.
Results	
Value:	LD_{50} was >5,000 mg/kg (males) and approx. 2812 mg/kg for females
Deaths at each dose:	5,000 mg/kg: 2 males (Day 1) and 5 females (4 on Day 1 and 1 on Day 2).
Remarks:	Animals showed slight to severe weakness with prostration and diarrhea on Day 0. By Day 2 all surviving males appeared clinically normal. 4,000 mg/kg: 3/5 died on Day 1 and the other 2 died on Day 2. On day 0, animals exhibited slight to moderate weakness progressing to moderate weakness with reduced feces by Day 2. 2,500 mg/kg: 1/5 died on Day 1. Day 0, one animal exhibited slight weakness while all the others were clinically normal throughout the study. A gain in weight was reported for all survivors after the 2-week study observation period was complete. The cause of death for the rats was not determined although results of the gross necropsies indicated evidence of gastric irritation.
Conclusions	Material would be considered as slightly toxic.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	The study followed established guidelines and was conducted under GLP assurances.
References	Dimethyl-1,4-cyclohexanedicarboxylate, mixed isomer acute oral toxicity in the rat. Eastman Kodak Company, Rochester, NY; HAEL No.: 95-0212; January 9, 1996.
Other	The results of an acute toxicity study conducted on the *trans* isomer of DMCD (CAS No. 3399-22-2) indicated the LD_{50} as >3,200 mg/kg for both sexes with no evidence of toxicity. [Basic toxicity of trans-Dimethyl-1,4-cyclohexanedicarboxylate; Eastman Kodak Company, Rochester, NY; HS&HFL No.: 80-0296; February 18, 1981

B. Repeated Dose Toxicity

Test Substance	
Test substance:	1,4-Cyclohexanedicarboxylic acid (CHDA; CAS No.: 1076-97-7)
Remarks:	Purity was 99.0%
Method	
Method:	OECD: TG-407 and Annex V B.7
Test type:	Repeated oral-dose toxicity
GLP:	Yes
Year:	1988
Species/strain:	Rat/Sprague-Dawley (CD(SD)BR)
Route of exposure:	Oral
Duration of test:	4-weeks
Exposure levels:	0, 0.1, 0.3, and 1.0% in diet
Sex:	Both (5/sex)
Exposure period:	Continuous in feed for 29 days
Post-exposure observation period:	None
Remarks:	Rats, were approximately 6-7 weeks in age and weighed 177 g (males) and 143 g (females) at study initiation. Animals were weighed and had detailed clinical observations recorded on Days 0, 4, 7, 14, 18, 22, and 29. Feed intake was assessed twice/week. At termination hematology (Hb conc., Hct, RBC count and morphology, WBC count and diff., and plt. Count) and clinical chemistries (AST, ALT, SDH, ALK, Creat., BUN, and gluc.) were conducted. At termination, animals underwent a gross examination with the following organs weighed: liver, spleen, kidneys, adrenals, testes, and thymus. Organs examined by histology included: trachea, lungs, heart, esophagus, stomach, sm. & lg. intestine, pancreas, liver, salivary glands, kidney, urinary bladder, pituitary, adrenals, thyroids, parathyroids, thymus, spleen, mesenteric lymph nodes, bone marrow, brain, testes, epididymis, accessory sex organs in males, fallopian tubes, uterus, vagina and ovaries.
Results	
NOAEL (NOEL):	1.0%; [871 mg/kg (males) and 894 mg/kg (females)]
Actual doses received:	Males: 0, 81, 246, 871 mg/kg; Females: 0, 86, 259, 894 mg/kg
Toxic responses by dose:	There were no mortalities or clinical signs related to exposure. There were no differences in body weights, feed consumption, hematology, clinical chemistries, and organ weights compared to controls. There were no gross or histological changes observed.
Statistical methods:	Mean values of most data were evaluated for homogeneity by Bartlett's test and significance assessed using ANOVA and Duncan's multiple range test.
Remarks:	
Conclusions	CHDA induced essentially no toxicity following 4 weeks of exposure at a high exposure rate (1% of diet).
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This is a well-documented study that followed OECD guidelines and was conducted under GLP assurances.
References	Four-Week Oral Toxicity Study of 1,4-Cyclohexanedicarboxylic Acid in the Rat. Eastman Kodak Company, Rochester, NY; HAEL No.: 87-0082, Experiment No.: 870082F1, January 8, 1988.
Other	

Test Substance	
Test substance:	DMCD (*trans* isomer); CAS No.: 3399-22-2
Remarks:	Purity was unknown, material was stated to have 1.6% of the *cis*- isomer
Method	
Method:	Other
Test type:	Repeated oral-dose toxicity
GLP:	No
Year:	1981
Species/strain:	Rat/
Route of exposure:	Oral
Duration of test:	2-Weeks
Exposure levels:	0, 0.1 and 1.0% in diet
Sex:	Male
Exposure period:	Continuous in feed for 12 days
Post-exposure observation period:	None
Remarks:	Five rats were exposed to trans-DMCD in their diet. Observations were made of body weight, feed consumption, clinical signs, hematology (Hb conc., Hct, RBC count and morphology, WBC count and diff.) and clinical chemistries (AST, ALT, LDH, ALK, Creat., BUN, and gluc.) were conducted. At termination, animals underwent a gross examination with the liver and kidneys weighed and examined histologically.
Results	
NOAEL (NOEL):	1.0%; 1000 mg/kg
Actual doses received:	0, 97, and 1000 mg/kg
Toxic responses by dose:	There were no mortalities or clinical signs related to exposure. There were no differences in body weights, feed consumption, hematology, clinical chemistries, and organ weights compared to controls. There were no gross or histological changes observed.
Statistical methods:	Not described.
Remarks:	
Conclusions	Trans-DMCD induced essentially no toxicity following 2 weeks of exposure at a high exposure rate (1% of diet).
Data Quality	
Reliability:	Reliable with restrictions
Remarks:	Only basic data as part of a report summary were available for this study and significant methodological details were not present.
References	Basic Toxicity of *trans*-Dimethyl-1,4-cyclohexanedicarboxylate. Eastman Kodak Company, Rochester, NY; HS&HFL No.: 80-0296, February 18, 1981.
Other	

C. Genetic Toxicity - Mutation

Test Substance	
Test substance:	1,4-Cyclohexanedicarboxylic acid (CHDA; CAS No.: 1076-97-7)
Remarks:	Purity unknown
Method	
Method:	Other; OECD: TG-471-like
Test type:	*In vitro* mutagenicity
GLP:	Yes
Year:	1994
Species/strain:	*Salmonella typhimurium* (strains: TA98, 100, 1535, and 1537) and Escherichia *coli* (strain: WP2*uvr*A(pKM101)
Metabolic activation:	Yes; Sprague-Dawley rat liver S9 induced with Aroclor 1254
Concentration tested:	100, 333, 667, 1,000, 3,330, and 5,000 ug/plate
Remarks:	Positive controls: 2-aminoanthracene, 2-nitrofluorene, sodium azide, ICR-191, 4-nitroquinoline-N-oxide. Negative control was the test vehicle dimethylsulfoxide. The study was performed in triplicate at each dose.
Results	
Result:	No positive responses were induced by CHDA in any of the tester strains
Cytotoxic concentration:	No cytotoxicity was observed
Precipitation concentration:	No precipitate was noted.
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	Specific methods were not noted in the report. However, analyses were not needed due to the absence of an increase in the number of revertants colonies at any dose beyond the positive control.
Remarks:	
Conclusions	Material was not genotoxic under conditions of this assay.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was well-documented study that followed the basic principles of those outlined in OECD guideline 471 and was conducted under GLP assurances. Data were missing on sample purity.
References	Mutagenicity Test with EC 94-0212, CHDA in the Salmonella – Escherichia coli/Mammalian-Microsome Reverse Mutation Assay with a Confirmatory Assay; Hazelton Washington, Vienna, VA; HWA Study No.: 16281-0-409R; September 19, 1994.
Other	

D. Genetic Toxicity – Chromosomal Aberrations

Test Substance	
Test substance:	1,4-Cyclohexanedicarboxylic acid (CHDA; CAS No.: 1076-97-7)
Remarks:	Purity unknown
Method	
Method:	Similar to OECD: TG-473
Test type:	*In vitro* mammalian chromosomal aberrations assay
GLP:	Yes
Year:	1994
Species/strain:	Chinese hamster ovary cells (CHO)
Concentrations tested:	750, 1,000, 1,500, and 2,000 ug/ml
Metabolic Activation:	Aroclor 1254-induced SD rat liver S9
Remarks:	The positive controls consisted of mitomycin-C and cyclophosphamide. Negative control was the test vehicle dimethylsulfoxide. Assay length was 20.0 hours. Replicate cultures were used at each dose level. Mitotic index was based on metaphase analysis of 1000 cells and aberrations were based on a scoring of 100 cells from each replicate or 200 total.
Results	
Result:	No significant increase in cells with aberrations was observed (see remarks)
Cytotoxic concentration:	Evidence of cytotoxicity was seen at 2,250 ug/ml
Precipitation concentration:	A precipitate was observed at the 2,250 ug/ml concentration
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	Statistical analysis employed a test for linear trends and Fisher's Exact Test to compare the percentage of cells with aberrations with an adjustment for multiple comparisons.
Remarks:	A confirmatory assay was conducted at dose levels of 500, 1,000, 1,500, 2,000, and 2,250 ug/ml with cells harvested after 20 and 44 hours. Complete toxicity was seen at 2,250 ug/ml without metabolic activation. No increases in aberrations were seen after 20 hours in the non-activation system or at 44 hours with S9 at any dose. However, an increase in aberrations was seen in one of the replicates at the 2,000 ug/ml dose (-S9) at the 44-hour time point and at the 2,250 ug/ml dose with S9 after 20 hours. A significant increase in percent polyploidy was observed at 2,250 ug/ml from the 44-hour assay with activation.
Conclusions	No dose relationship was observed in the assays where a positive response was observed. The positive response for aberrations was observed in only one of the replicate cultures while the Polyploidy response was seen in both. However, severe toxicity was seen at this concentration. Accordingly, the relevance of these effects at a toxic concentration makes its significance questionable.
Data Quality	
Reliability:	Reliable without restrictions
Remarks:	This was well-documented study that followed the basic principles of those outlined in OECD guideline 473 and was conducted under GLP assurances. Data were missing on sample purity.
References	Measuring Chromosomal Aberrations in Chinese Hamster Ovary Cells; Hazelton Washington, Vienna, VA; HWA Study No.: 16281-0-437CO; November 1, 1994
Other	

E. Developmental Toxicity

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	Purity was 93.2%
Method	
Method:	OECD:TG-421; USEPA: OPPTS 870.3550
GLP:	Yes
Year:	2003
Species/strain:	Rats/Sprague-Dawley CRL:CD®(SD)IGS BR
Sex:	Male and Female (12/sex/exposure level)
Route of exposure:	Oral, dietary
Exposure levels:	0, 1.5, 4.5, and 15.0 mg/g of feed (0.15, 0.45, and 1.5%)
Actual dose levels:	Approx. 92, 276, and 888 mg/kg (male), and 111, 351, and 1124 mg/kg (female)
Exposure period:	24 hrs/day; Test material in diet was fed *ad libitum*
Frequency of treatment:	7 days/week
Control group and treatment:	Controls were exposed to basal diet
Duration of test:	The study consisted of four phases: pre-mating (14 days); mating (1 to 14 days); pregnancy (21 to 23 days); and early lactation (4 to 6 days). The male rats were treated throughout the study, a period of 50 days. The female rats were treated throughout the study until they were euthanized, a period of approximately 38-57 days. The male rats were euthanized on Day 51. The female rats that delivered a litter, and their offspring, were euthanized on Days 4, 5, or 6 postpartum. Female rats that showed evidence of mating but did not deliver were euthanized on Day 23 of gestation.
Remarks:	The study design included the additional endpoints of epididymal spermatozoan numbers and motility, and testicular spermatid head counts.
Results	
Maternal/Paternal toxicity	
NOAEL:	1.5%; or 888 mg/kg for males and 1124 mg/kg for females
Repro./Develop. toxicity	
NOAEL:	1.5%; or 888 mg/kg for males and 1124 mg/kg for females
Parental toxic responses:	Male rats that consumed diets containing 15.0 mg/g (1.50%) of the test substance exhibited reduced mean body weights and/or feed consumption values for the duration of the study. However, there were no adverse effects on fertility, histology of the testes and epididymis, or testicular and epididymal sperm counts. No treatment-related effects were seen in male rats from the lower dose groups. There were no treatment-related effects or histopathological alterations seen in female rats from any dose group and there were no biologically significant changes in their offspring.
Postnatal toxic responses:	There were no toxicologically significant differences in the reproductive parameters evaluated including reproductive performance, fertility index, fecundity index, precoital interval, gestation duration, numbers of implants, number of corpora lutea, pre- and post-implantation loss, pup survival, live and dead pups, male and female pups, pup body weight and body weight changes. Although the duration of the gestation phase was shorter ($p \leq 0.05$) for female rats from the mid-dose group, there was no apparent effect on pup viability. Mean pup weight change and percent pup weight change from Days 0 to 4 were also significantly ($p \leq 0.05$) higher for pups from the low-dose group when compared with the control group, but these changes were not considered biologically significant.

Statistical Methods:	Homogeneity of data was evaluated using Bartlett's test ($p \leq 0.01$), one-way analysis of variance (ANOVA) ($p \leq 0.05$), and Dunnett's t-test ($p \leq 0.05$) to indicate statistical significance. When the variances of the means were not considered equal by the Bartlett's test ($p \leq 0.01$), the data were evaluated using a Kruskal-Wallis H-test ($p < 0.05$) followed by Mann-Whitney U-test ($p < 0.05$).
Remarks:	The reproductive performance of the dams and the fertility and fecundity indices were evaluated in contingency tables, using a Chi-square test ($p < 0.05$).
Conclusions	DMCD did not affect the reproductive capacity of the adult animals in this study.
Data Quality	
Reliability:	Reliable without restriction
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Reproduction/Developmental Toxicity Screening Test in the Rat. Toxicological Sciences Laboratory; Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; July 2003.
Other	

F. Reproductive Toxicity

Test Substance	
Test substance:	DMCD (mixed isomers); CAS No.: 94-60-0
Remarks:	Purity was 93.2%
Method	
Method:	OECD:TG-421; USEPA: OPPTS 870.3550
GLP:	Yes
Year:	2003
Species/strain:	Rats/Sprague-Dawley CRL:CD®(SD)IGS BR
Sex:	Male and Female (12/sex/exposure level)
Route of exposure:	Oral, dietary
Exposure levels:	0, 1.5, 4.5, and 15.0 mg/g of feed (0.15, 0.45, and 1.5%)
Actual dose levels:	Approx. 92, 276, and 888 mg/kg (male), and 111, 351, and 1124 mg/kg (female)
Exposure period:	24 hrs/day; Test material in diet was fed *ad libitum*
Frequency of treatment:	7 days/week
Control group and treatment:	Controls were exposed to basal diet
Duration of test:	The study consisted of four phases: pre-mating (14 days); mating (1 to 14 days); pregnancy (21 to 23 days); and early lactation (4 to 6 days). The male rats were treated throughout the study, a period of 50 days. The female rats were treated throughout the study until they were euthanized, a period of approximately 38-57 days. The male rats were euthanized on Day 51. The female rats that delivered a litter, and their offspring, were euthanized on Days 4, 5, or 6 postpartum. Female rats that showed evidence of mating but did not deliver were euthanized on Day 23 of gestation.
Remarks:	The study design included the additional endpoints of epididymal spermatozoan numbers and motility, and testicular spermatid head counts.
Results	
Maternal/Paternal toxicity	
NOAEL:	1.5%; or 888 mg/kg for males and 1124 mg/kg for females
Repro./Develop. toxicity	
NOAEL:	1.5%; or 888 mg/kg for males and 1124 mg/kg for females
Parental toxic responses:	Male rats that consumed diets containing 15.0 mg/g (1.50%) of the test substance exhibited reduced mean body weights and/or feed consumption values for the duration of the study. However, there were no adverse effects on fertility, histology of the testes and epididymis, or testicular and epididymal sperm counts. No treatment-related effects were seen in male rats from the lower dose groups. There were no treatment-related effects or histopathological alterations seen in female rats from any dose group and there were no biologically significant changes in their offspring.
Postnatal toxic responses:	There were no toxicologically significant differences in the reproductive parameters evaluated including reproductive performance, fertility index, fecundity index, precoital interval, gestation duration, numbers of implants, number of corpora lutea, pre- and post-implantation loss, pup survival, live and dead pups, male and female pups, pup body weight and body weight changes. Although the duration of the gestation phase was shorter ($p \leq 0.05$) for female rats from the mid-dose group, there was no apparent effect on pup viability. Mean pup weight change and percent pup weight change from Days 0 to 4 were also significantly ($p \leq 0.05$) higher for pups from the low-dose group when compared with the control group, but these changes were not considered biologically significant.

Statistical Methods:	Homogeneity of data was evaluated using Bartlett's test ($p \leq 0.01$), one-way analysis of variance (ANOVA) ($p \leq 0.05$), and Dunnett's t-test ($p \leq 0.05$) to indicate statistical significance. When the variances of the means were not considered equal by the Bartlett's test ($p \leq 0.01$), the data were evaluated using a Kruskal-Wallis H-test ($p < 0.05$) followed by Mann-Whitney U-test ($p < 0.05$).
Remarks:	The reproductive performance of the dams and the fertility and fecundity indices were evaluated in contingency tables, using a Chi-square test ($p < 0.05$).
Conclusions	DMCD did not affect the reproductive capacity of the adult animals in this study.
Data Quality	
Reliability:	Reliable without restriction
Remarks:	This was a well-documented OECD guideline study conducted under GLP assurances.
References	Reproduction/Developmental Toxicity Screening Test in the Rat. Toxicological Sciences Laboratory; Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY; July 2003.
Other	